April 13, 2021

Immunodiagnostic Systems Ltd.
Mick Henderson
Regulatory Affairs Manager
10 Didcot Way Boldon Business Park
Boldon, Tyne and Wear NE35 9PD
United Kingdom

Re: K202136
Trade/Device Name: IDS Cortisol
Regulation Number: 21 CFR 862.1205
Regulation Name: Cortisol (Hydrocortisone And Hydroxycorticosterone) Test System
Regulatory Class: Class II
Product Code: CGR
Dated: October 8, 2020
Received: October 13, 2020

Dear Mick Henderson:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. Although this letter refers to your product as a device, please be aware that some cleared products may instead be combination products. The 510(k) Premarket Notification Database located at https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm identifies combination product submissions. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal

statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part 801 and Part 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803) for devices or postmarketing safety reporting (21 CFR 4, Subpart B) for combination products (see https://www.fda.gov/combination-products/guidance-regulatory-information/postmarketing-safety-reporting-combination-products); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820) for devices or current good manufacturing practices (21 CFR 4, Subpart A) for combination products; and, if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to https://www.fda.gov/medical-devices/medical-device-safety/medical-device-reporting-mdr-how-report-medical-device-problems.

For comprehensive regulatory information about medical devices and radiation-emitting products, including information about labeling regulations, please see Device Advice (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance) and CDRH Learn (https://www.fda.gov/training-and-continuing-education/cdrh-learn). Additionally, you may contact the Division of Industry and Consumer Education (DICE) to ask a question about a specific regulatory topic. See the DICE website (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/contact-us-division-industry-and-consumer-education-dice) for more information or contact DICE by email (DICE@fda.hhs.gov) or phone (1-800-638-2041 or 301-796-7100).

Sincerely,

Kellie B. Kelm -S

Kellie B. Kelm
Director
Division of Chemistry and Toxicology Devices
OHT7: Office of In Vitro Diagnostics and Radiological Health
Office of Product Evaluation and Quality
Center for Devices and Radiological Health

Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: 06/30/2023
See PRA Statement below.

510(k) Number *(if known)*
K202136

Device Name
IDS Cortisol

Indications for Use *(Describe)*
The IDS Cortisol assay is an in vitro diagnostic device intended for the quantitative determination of cortisol in human serum and plasma on the IDS system. Results are to be used in conjunction with other clinical and laboratory data to assist clinicians in the diagnosis and treatment of disorders of the adrenal gland.

Type of Use *(Select one or both, as applicable)*

☒ Prescription Use (Part 21 CFR 801 Subpart D) ☐ Over-The-Counter Use (21 CFR 801 Subpart C)

CONTINUE ON A SEPARATE PAGE IF NEEDED.

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510(k) SUMMARY

510k Number k202136

Introduction According to the requirements of 21CFR807.92, the following information provides sufficient detail to understand the basis for a determination of substantial equivalence.

Submitter

Immunodiagnostic Systems Limited
10 Didcot Way
Boldon Business Park
Boldon
Tyne and Wear
NE35 9PD
United Kingdom

Contact Person: Mick Henderson
Phone: +44 191 5190660
Fax: +44 191 5190760
Email: mick.henderson@idsplc.com

Secondary Contact: Lee Harris
Phone: +44 191 5190660
Fax: +44 191 5190760
Email : lee.harris@idsplc.com

Date prepared: 27 July 2020

Device Name

Proprietary names:	IDS Cortisol
Common names:	As above
Classification:	21CFR862.1205 Cortisol (hydrocortisone and hydroxycorticosterone) test system. Class II
Product Code:	CGR

Predicate Device The IDS Cortisol is substantially equivalent to other products in commercial distribution intended for similar use. We claim equivalency to the currently marketed Roche Elecsys Cortisol II (k152227).

Device Description The IDS Cortisol assay consists of a reagent cartridge. The reagent cartridge contains multiple reagents:

- MPE1:Magnetic particles coated rat anti-mouse monoclonal antibody in a phosphate buffer with Proclin as preservative.
- CONJ: Cortisol coupled with an acridinium ester derivative in phosphate buffer with Proclin as a preservative.
- mAb: Mouse anti-cortisol monoclonal antibody in phosphate buffer with Proclin as a preservative.;
- BUF: HEPES buffer containing Proclin as preservative .

Indications for Use

The IDS Cortisol assay is an *in vitro* diagnostic device intended for the quantitative determination of cortisol in human serum and plasma on the IDS system. Results are to be used in conjunction with other clinical and laboratory data to assist clinicians in the diagnosis and treatment of disorders of the adrenal gland.

Conditions for use: For in vitro diagnostic use only.
Rx Only

Special instrument Requirements:

IDS-iSYS Multi-Discipline Automated System (k091849)

Comparison Tables

Similarities compared to the chosen (FDA cleared; marketed) predicate device (k152227)

Assay Performance	**Predicate Device Roche Elecsys Cortisol II (k152227)**	**Candidate Device IDS Cortisol**
Intended Use	For quantitative determination of Cortisol	same
Method of detection (Test methodology)	chemiluminescence	same

Differences compared to the chosen (FDA cleared; marketed) predicate device (k152227)

Performance	**Predicate Device Roche Elecsys Cortisol II (k152227)**	**Candidate Device IDS Cortisol**
Indications for Use	Immunoassay for the in vitro quantitative determination of cortisol in human serum, plasma, urine and saliva. The determination of cortisol is used for the recognition and treatment of functional disorders of the adrenal gland. The electrochemiluminescence immunoassay "ECLIA" is intended for use on Elecsys and cobas e immunoassay	The IDS Cortisol assay is an *in vitro* diagnostic device intended for the quantitative determination of cortisol in human serum and plasma on the IDS system. Results are to be used in conjunction with other clinical and laboratory data to assist clinicians in the diagnosis and treatment of disorders of the adrenal gland.
Sample Type	Human Serum, plasma, urine and saliva	Human Serum and plasma
Sample Volume	10 µL	30 µL
Range of assay	3 – 1750 nmol/L (0.109 to 63.4 µg/dL)	0.59 – 45 µg/dL

Sensitivity	LoB 1.0 nmol/L (0.036 µg/dL) LoD 1.5 nmol/L (0.054 µg/dL) LoQ 3.0 nmol/L (0.109 µg/dL)	LoB 0.1 µg/dL LoD 0.24 µg/dL LoQ 0.59 µg/dL
Expected values	Morning hours 6-10am 95th percentile 6.02-18.4 µg/dL Afternoon hours 4-8pm 95th percentile 2.68-10.5 µgd/L	Morning hours 6-10am 95th percentile 4.23-20.1 µg/dL Afternoon hours 4-8pm 95th percentile 2.37-13.6 µg/dL
Precision	<u>Repeatability n =84</u> 1.4% to 7.1% in the concentration range 0.112 to 57.7 µg/dL <u>Intermediate Precision n = 84</u> 2.5% to 12.7% in the concentration range 0.014 to 0.653 µg/dL	<u>Within Run / Repeatability Precision n =80</u> 1.8% to 7.8% in the concentration range 0.94 to 44.63 µg/dL <u>Within System n = 80</u> 3.9% to 16.2% in the concentration range 0.94 to 44.63 µg/L
Specificity, Interfering substances And Cross Reactivity	<u>Interfering Substances</u> Bilirubin 25 mg/dL Biotin 30ng/mL Haemoglobin No Claim Human Anti Mouse Antibody (HAMA) No Claim Rheumatoid Factor 600IU/mL Total Protein No Claim Triglycerides No Claim Acetaminophen No Claim Carbamezapine No Claim Ibuprofen No Claim Phenytoin No Claim	<u>Interfering Substances</u> Bilirubin – conjugated 40 mg/dL Bilirubin – unconjugated 40 mg/dL Biotin 6 µg/dL Haemoglobin 500 mg/dL Human Anti Mouse Antibody (HAMA) 1000 ng/dL Rheumatoid Factor 2000IU/mL Total Protein 12 g/dL Triglycerides 3000mg/dL Acetaminophen 200 µg/mL Carbamezapine 30 µg/mL Ibuprofen 500 µg/mL Phenytoin 50 µg/dL

	Cross Reactivity 11-Deoxycorticosterone 10µg/L yields a result of 0.64% 11-Deoxycortisol 10µg/L yields a result of 4.9% 17-a-Hydroxyprogesterone 10µg/L yields a result of 0.08% Corticosterone 10µg/L yields a result of 2.48% Cortisone 10µg/L yields a result of 6.58% Dexamethasone 10µg/L yields a result of not detectable Prednisone 10µg/L yields a result of 2.23% Progesterone 10µg/L yields a result of 0.035% 21-Deoxycortisol 1µg/L yields a result of 2.4% Prednisolone 0.1µg/L yields a result of 7.98% 6-a-Methylprednisolone 0.1µg/L yields a result of 12.0%	Cross Reactivity 11-Deoxycorticosterone 1000µg/dL yields a result of 2.2% 11-Deoxycortisol 100µg/dL yields a result of 11.5% 17-a-Hydroxyprogesterone 1000µg/dL yields a result of 2.6% Corticosterone 100µg/dL yields a result of 19.9% Cortisone 100µg/dL yields a result of 36.5% Dexamethasone 1000µg/dL yields a result of 1.4% Prednisone 100µg/dL yields a result of 43.5% Progesterone 1000µg/dL yields a result of 0.3% 21-Deoxycortisol 100µg/dL yields a result of 37% Prednisolone 50µg/dL yields a result of 51.3% 6-a-Methylprednisolone 10µg/dL yields a result of 0%

Method comparison	Against Elecsys Cortisol (k070788): n = 536 Elecsys Cortisol II = 0.76 x (Elecsys Cortisol) -1.85 µg/L Correlation coefficient (r) = 0.968	Against Elecsys Cortisol II (k152227): n = 194 IDS Cortisol = 1.06 x (Roche Elecsys Cortisol II) - 0.10 µg/dL Correlation coefficient (r) = 0.99
Linearity	3.0 to 1750 nmol/L	0.59 – 45 µg/dL Observed = 1.01 x (Expected) +0.01 µg/dL Regression coefficient R^2: 1.00

Performance Characteristics (if/when applicable):

1. Analytical performance:

a. Precision/Reproducibility:

Precision was evaluated in accordance with a modified protocol based on CLSI EP-5A3, "Evaluation of Precision Performance of Quantitative Measurement Methods". A total of 6 samples were assayed using 3 lots of reagents in duplicate, twice a day for 20 days on 3 systems. The IDS Cortisol assay precision was established using samples with concentrations ranging from approximately 0.80 µg/dL to 46.00 µg/dL.

Results from 1 representative lot on 1 system:

Sample	N	Mean Conc. (µg/dL)	Repeatability		Within system	
			SD	CV	SD	CV
1	80	0.94	0.07	7.8%	0.15	16.2%
2	80	1.84	0.08	4.6%	0.20	10.9%
3	80	5.75	0.14	2.4%	0.30	5.2%
4	80	13.06	0.31	2.4%	0.52	3.9%
5	80	19.94	0.36	1.8%	1.02	5.1%
6	80	44.63	0.85	1.9%	1.89	4.2%

Results for the combined 3 lots on 3 systems:

Sample	N	Mean Conc. (µg/dL)	Within run		Total	
			SD	CV	SD	CV
1	240	0.88	0.06	7.1%	0.14	15.3%
2	240	1.78	0.08	4.3%	0.18	10.1%
3	240	5.75	0.13	2.3%	0.26	4.5%
4	240	13.09	0.25	1.9%	0.43	3.3%
5	240	20.22	0.35	1.7%	0.96	4.8%
6	240	44.48	0.74	1.7%	2.22	5.0%

b. Linearity/assay reportable range:

A linearity study was conducted based on guidance from the CLSI EP6-A. A high human serum sample and a low human serum sample were prepared respectively by spiking a serum sample with Cortisol high concentration solution and diluting a serum sample with Cortisol zero matrix. High and a low serum samples were analysed in addition to 12 evenly spaced dilutions which were created by mixing the high and low sample as indicated below:

Sample	Dilution	Dilution Factor (%)
1:	Low (L)	0
2:	0.98L + 0.02H	2
3:	0.95L + 0.05H	5
4:	0.92L + 0.08H	8
5:	0.90L + 0.10H	10
6:	0.80L + 0.20H	20
7:	0.70L + 0.30H	30
8:	0.60L + 0.40H	40
9:	0.50L + 0.50H	50
10:	0.40L + 0.60H	60
11:	0.30L + 0.70H	70
12:	0.20L + 0.80H	80
13:	0.10L + 0.90H	90
14:	High (H)	100

Results:

Linearity was evaluated based on CLSI EP-6A, "Evaluation of the Linearity of Quantitative Measurement Procedures". Samples were prepared by diluting a high patient sample with a low patient sample prior to assay. The linear regression of the observed concentrations versus the expected concentrations is:

Observed = 1.01 x (Expected) + 0.01 µg/dL; Regression coefficient R^2: 1.00

The IDS Cortisol assay is linear over the measuring range 0.59 to 45.00 µg/dL

c. Traceability, Stability, Expected values (controls, calibrators, or methods):

Traceability

The IDS Cortisol assay is traceable to the LC-MS/MS Candidate Reference Measurement Procedure (cRMP) Total Serum Cortisol. Through analysis of a Joint Committee for Traceability in Laboratory Medicine (JCTLM)-listed panel of higher-order Candidate Reference Materials (CRM), the IDS Cortisol provided metrologically traceable results.

Stability

The stability based on accelerated stability studies determined a shelf life of 12 months

d. Detection limit:

The limit of blank (LoB), limit of detection (LoD) and limit of quantitation (LoQ) were determined with guidance from CLSI EP17A2, "Protocols for Determination of Limits of Detection and Limits of Quantitation" using 60 blank replicates and 13 low level samples.

Sensitivity	**Concentration (µg/dL)**
Limit of Blank (LoB)	0.10
Limit of Detection (LoD)	0.24
Limit of Quantitation (LoQ)	0.59

e. Analytical specificity:

Interference and cross-reactivity studies were performed in accordance with the CLSI EP07-A3 Interference.

The potential interference of each substance in the specific detection of Cortisol, with the exception of Rheumatoid Factor (see the description of the Rheumatoid Factor interference), was tested using human serum samples with low and high cortisol concentrations. Interference substances were spiked into the serum samples and the results were measured and compared between the spiked and unspiked samples.

% Interference was calculated using the following formula:

$$\% \text{ Interference} = \frac{(\text{mean spiked concentration} - \text{mean unspiked concentration})}{\text{mean unspiked concentration}} \times 100$$

To determine potential interference of Rheumatoid Factor, a serum sample with low Cortisol and high Rheumatoid Factor concentration was diluted 1:2 and 1:4 in cortisol zero matrix and each dilution was assayed in duplicate. Linearity on dilution was assessed.

% Observed/Expected (%O/E) was calculated using the following formula:

$$\% \text{ O/E} = \frac{\text{observed mean concentration}}{\text{expected concentration}} \times 100$$

The following compounds were tested and found not to interfere significantly with the test, based on the predefined acceptance criteria of non-significant interference of <10% bias between the test and control samples:

Potentially Interfering Agent	Threshold Concentration
Acetaminophen	200 µg/mL
Bilirubin (Conjugated)	40 mg/dL
Bilirubin (Unconjugated)	40 mg/dL
Biotin	6 µg/mL
Carbamezapine	30 µg/mL
Haemoglobin	500 mg/dL
HAMA	1000 ng/mL
Ibuprofen	500 µg/mL
Phenytoin	50 µg/mL
RhF	2000 IU/mL
Total protein	12 g/dL
Triglycerides	3000 mg/dL

Cross-reactivity testing was performed for Cortisone, Corticosterone, Dexamethasone, Prednisone, Prednisolone, 21-deoxycortisol, 6-a-Methylprednisolone, 17-a-Hydroxyprogesterone, 6-b-Hydroxycortisol, Progesterone, 11-Deoxycortisol, 11-Deoxycorticosterone, Aldosterone.

For each serum sample spiked with a cross-reactant, a control (unspiked sample) was prepared by replacing the cross-reactant with the same volume of cross-reactant solvent. Both spiked and unspiked samples were assayed in 26 replicates each.

The cross reactivity was determined using the formula below:

$$\% \text{ cross reactivity} = \frac{(\text{Mean conc. of spiked sample} - \text{mean conc. of un-spiked sample})}{\text{Final concentration of cross-reactant added}} \times 100\%$$

Potentially Cross reactant	Tested Concentration	% cross reactivity
Aldosterone	1000 µg/dL	0.0
Cortisone	100 µg/dL	36.5
Corticosterone	100 µg/dL	19.9
Dexamethasone	1000 µg/dL	1.4
Prednisone	100 µg/dL	43.5
Prednisolone	50 µg/dL	51.3
21-deoxycortisol	100 µg/dL	37.0
6-a-Methylprednisolone	10 µg/dL	-0.4
17-a-Hydroxyprogesterone	1000 µg/dL	2.6
6-b-Hydroxycortisol	100 µg/dL	0.4
Progesterone	1000 µg/dL	0.3
11-Deoxycortisol	100 µg/dL	11.5
11-Deoxycorticosterone	1000 µg/dL	2.2

f. Assay cut-off:

Not applicable

2. Comparison studies:

a. Method comparison against the predicate device:

The IDS Cortisol assay was compared against the Roche Elecsys Cortisol II for the quantitative determination of Cortisol, following CLSI EP-9A3, "Method Comparison and Bias Estimation Using Patient Samples". A total of 194 samples, selected to represent a wide range of Cortisol concentrations [0.64 to 44.66 µg/dL], were assayed by each method. Passing-Bablok regression analysis was performed on the comparative data:

n	Slope	95% CI	Intercept (µg/dL)	95% CI	Correlation Coefficient (r)
194	1.06	1.04 to 1.07	-0.10	-0.39 to 0.04	0.99

b. Matrix comparison:

The IDS Cortisol matrix comparison study was performed to evaluate the difference across tube types (serum separator tubes (SST), lithium heparin plasma, sodium heparin plasma, K2 EDTA plasma and K3 EDTA plasma) versus the control samples (red top serum, without additive) following the CLSI EP9-A3 guideline. A total of 45 samples (36 native, 9 spiked or diluted) to cover the range of 0.89 to 42.38 µg/dL. Passing-Bablok regression analysis was performed on the comparative data:

Sample type	N	Slope	95% CI	Intercept (µg/dL)	95% CI	Corr. Coeff. (r)
SST	45	1.02	0.99 to 1.03	-0.08	-0.18 to 0.10	1.00
K_2 EDTA	45	1.03	1.01 to 1.04	-0.11	-0.23 to 0.03	1.00
K_3 EDTA	45	1.02	0.99 to 1.03	-0.10	-0.29 to 0.08	1.00
Lithium Heparin	45	1.00	0.99 to 1.02	0.15	-0.01 to 0.33	1.00
Sodium Heparin	45	1.01	1.00 to 1.03	0.00	-0.16 to 0.18	1.00

3. Expected values/Reference range:

The cortisol concentration was measured in serum samples collected from 307 apparently healthy donors using the IDS Cortisol assay. The study cohort included subjects from 21 to 65 years of age, with normal blood pressure (120/80) and normal BMI, (18.5 to 29.0). Individuals who were pregnant, breast feeding, had personal history of chronic disease, under any prescription medication or any doctor prescribed diet were excluded from the study. The 95 % reference intervals for apparently healthy adults were calculated by a non-parametric method following guidance from CLSI C28-A3 "Defining, Establishing and Verifying Reference Intervals in the Clinical Laboratory".

The package insert recommends that 'Each laboratory should determine ranges for their local population.

	Morning hours 6 – 10 am	Afternoon hours 4 – 8 pm
Number of subjects	151	156
Mean µg/dL	11.6	7.46
SD (µg/dL)	3.88	2.81
Median µg/dL	11.3	7.15
Observed 2.5^{th} to 97.5^{th} percentile µg/dL	4.23-20.1	2.37-13.6

Conclusion:

The IDS Cortisol assay data presented and provided are complete and supports the basis for substantial equivalence to the predicate device.